

### REMARKS

Claims 57-103 are pending in the instant application and have been subject to a restriction requirement as follows:

**Group I:** Claims 57-99 and 104-107 drawn to a method for sequencing one or more target nucleic acids;

**Group II:** Claims 100, 102, and 108-114 drawn to kits for mass spectrometry sequencing.

Applicants provisionally elect the claims of Group I. Applicants respectfully **traverse** the restriction requirement.

#### **A. Group election and traversal**

The claims are directed to a method of sequencing by using mass spectrometry and the claims of group II provide specific compositions for use in those methods. The Examiner indicates the reasons for restriction are that:

“... the product as claimed can be used in a materially different process of using that product such as a method comprising steps of amplifying of a PCR product, purifying the PCR product, using ion exchange beads, cleaving the purified PCR product, hybridizing the cleaved PCR product with an array comprising a solid support, and analyzing hybridization results with a computer software.”

Applicants respectfully submit that the above reasons are not directed to the different uses of the product but merely recite uses for the individual components of the kits. However, the Applicants respectfully must point out that it is not those individual components that are the “product” identified by the Examiner or being claimed by the Applicants. The claims of group II of the invention are directed to kits. This “product” contains triphosphates, polymerases, nucleic acid cleaving agents, reference nucleic acids,

reagents for purification of PCR products, ion exchange beads, a solid support for use in mass spectrometry and a computer software program. Please note that the steps (a) through (h) of claim 100 are not alternative uses (as would be implied by the Examiner's rejection) but are rather separate components of the mass spectrometry kit. So again Applicants clarify that the "product" is the mass spectrometry "kit" not the individual components of the kit. For this reason, Applicants submit that the restriction is not proper and should be vacated.

**B. Species election, traversal and request for supervisory review**

The Examiner further required an election of species. Claims 57-62, 65-99 and 104-107 are generic. They are directed to a sequencing method that is performed using mass spectrometry. Applicants respectfully refer the examiner to the prior submissions (e.g., response dated March 26, 2004 in which it is explained that the methods of the invention:

“... have a number of steps that involve taking a target sequence and (1) subjecting it to at least two cleavage reactions to generate a non-ordered set of fragments; (2) analyzing the non-ordered fragments by mass spectrometry and (3) assembling the sequence of the target nucleic acid by performing a systematic computational analysis on the resultant mass spectra . . . to unambiguously determine the sequence of the target nucleic acid.”

The novelty and non-obviousness of the invention lies in the steps of the that demonstrate the use of mass spectrometry of non-ordered fragments generated from multiple cleavage reactions to deduce the sequence of a given target nucleic acid. Therefore, the specific control sequence (claims 63 and 64); the type of modified nucleotide triphosphate (claims 69, 70, 71, 72); the type of cleavage reaction (claims 75 and 77-80); or the nature of the target nucleic acid (claims 81, 82, 83, or 84) the type of RNase used (claims 106 and 107) is not the defining feature of the invention. For completeness Applicants are electing the following species:

Eukaryotic transcription control sequence (claim 63);

2'-deoxy, 2'-O-methyl, 2'-fluoro or 2'-amino substituent on the nucleotide triphosphates (claim 69);

Enzymatic cleavage (claims 75 and 78-80);

the one or more target nucleic acids are phosphorothioate-modified single stranded DNA or RNA, and wherein the cleavage reactions are performed with the nuclease P1 (claim 81)

the four RNase-specific cleavage reactions comprise RNase T1 and RNase U2 cleavage of the + and - strands of said target nucleic acid.

The above election of species is made with traverse and Applicants respectfully request and interview with the Examiner and the Examiner's supervisor to further discuss the nature of the restriction requirement and the status of the present case which has been pending since 2001.

Applicants believe that all of the rejections were previously overcome and the presently imposed restriction requirement is improper for the reasons presented above. As such Applicants request that the requirement be withdrawn and the claims be passed to allowance. The Examiner is invited to contact the undersigned with any questions, comments or suggestions relating to the referenced patent application.

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Respectfully submitted,

By 

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